

AMENDMENT UNDER 37 C.F.R. § 1.111

Amendments to the Specification:

Please replace paragraph [0085] with the following replacement paragraph:

Materials binding to AOP-1 mRNA or proteins or nucleic acids inhibiting the degradation of AOP-1 mRNA or materials having the activity of increasing the translation efficiency may also be included similarly to the production of ~~TNF~~ TNF- α known to be regulated by the post-transcriptional stability of mRNA and stabilized by binding of HuR protein.

Please replace paragraph [00120] with the following replacement paragraph:

The fragments of the protein of interest obtained in A above were analyzed as a mixture using a mass spectrometer from MicroMass (electrospray ionization time-of flight mass spectrometer) to give mass data of the fragments of the protein of interest. Some fragments were further irradiated with helium gas to cleave peptide bonds to give the internal sequence of the protein fragments N'[H(I/L)SVNDL] C' (SEQ ID NO: 31 and 32) and mass data (parent ion 1206.6, daughter ions 1069.481, 956.428, 869.418, 770.379, 656.336, 541.324, 428.244). Based on these data, AOP-1 was identified after searches through genetic sequence database available on the Internet (SwissProt Accession No. P20108: SEQ ID NO: 6).

Please replace paragraph [00121] with the following replacement paragraph:

Total RNA was prepared from each left ventricle using ISOGEN (Nippon Gene) as instructed by the manufacturer and treated with DNase. TaqMan® Reverse Transcription Reagents (PE Applied Biosystems) were used to synthesize cDNA from 1 µg each of the total RNA treated with DNase in 50 µl of the reaction solution. Gene expression was analyzed by a real-time PCR assay system using ABI PRISM 7700 (PE Applied Biosystems). The primers for detecting AOP-1 and the TaqMan® probe were designed on the basis of the nucleotide sequence of mouse AOP-1 cDNA using a primer design software ABI PRISM Primer Express. Forward primer 5'TGCAGTTTCAGTGGATTCCCA3' (SEQ ID NO: 7), reverse primer

5'TTCATGTGGCCCAAACCA3' (SEQ ID NO: 8), TaqMan® probe
5'TCTTGCCTGGATCAACACACCAAGAAAG3' (SEQ ID NO: 9).

Please replace paragraph [00123] with the following replacement paragraph:

Total RNA was prepared from each left ventricle using ISOGEN (Nippon Gene) as instructed by the manufacturer and treated with DNase. TaqMan® Reverse Transcription Reagents (PE Applied Biosystems) were used to synthesize cDNA from 1 µg each of the total RNA treated with DNase in 50 µl of the reaction solution. Gene expression was analyzed by a real-time PCR assay system using ABI PRISM 7700 (PE Applied Biosystems). The primers for detection and the TaqMan® probes were designed on the basis of the nucleotide sequences of rat TSA, CuZn-SOD, Mn-SOD and catalase cDNA using a primer design software ABI PRISM Primer Express. Rat TSA forward primer 5'CCCTCTGCTTGCTGATGTGACT3' (SEQ ID NO: 10), reverse primer 5'CCTGTAAGCGATGCCCTCAT3' (SEQ ID NO: 11), TaqMan® probe 5'AGCTTGTCCCAGAATTACGGCGTGTTGAA3' (SEQ ID NO: 12). CuZn-SOD forward primer 5'GCGGATGAAGAGAGGCATG3' (SEQ ID NO: 13), reverse primer 5'GCCACACCGTCC'TTTCCA3' (SEQ ID NO: 14), TaqMan® probe 5'TGGAGACCTGGGCAATGTGGCTG3' (SEQ ID NO: 15). Catalase forward primer 5'ACGGGTGCTCAGCCTCC3' (SEQ ID NO: 16), reverse primer 5'AGGCTTGTGCCCTGCTTC3' (SEQ ID NO: 17), TaqMan® probe 5'CAGCCTGCACTGAGGAGATCCCTCA3' (SEQ ID NO: 18). Mn-SOD forward primer 5'TTACAGATTGCCGCCTGCTC3' (SEQ ID NO: 21), reverse primer 5'CCAGCAGTGGAATAAGGCCT3' (SEQ ID NO: 22), TaqMan® probe 5'AATCACGACCCACTGCAAGGAACCA3'(SEQ ID NO: 23).

Please replace paragraph [00140] with the following replacement paragraph:

Total RNA was prepared from the tissue of each organ obtained in Example 10 above using ISOGEN (Nippon Gene) as instructed by the manufacturer and treated with DNase. TaqMan® Reverse Transcription Reagents (PE Applied Biosystems) were used to synthesize cDNA from 1 µg each of the total RNA treated with DNase in 50 µl of the reaction solution. Gene expression

was analyzed by a real-time PCR assay system using ABI PRISM 7700 (PE Applied Biosystems). The primers for detecting AOP-1 and other genes and the TaqMan® probe were designed on the basis of the nucleotide sequence of mouse AOP-1 cDNA using a primer design software ABI PRISM Primer Express. AOP-1 forward primer (SEQ ID NO: 7), reverse primer (SEQ ID NO: 8), TaqMan® probe (SEQ ID NO: 9). TSA forward primer (SEQ ID NO: 10), reverse primer (SEQ ID NO: 11), TaqMan® probe (SEQ ID NO: 12). CuZn-SOD forward primer (SEQ ID NO: 13), reverse primer (SEQ ID NO: 14), TaqMan® probe (SEQ ID NO: 15). Catalase forward primer (SEQ ID NO: 16), reverse primer (SEQ ID NO: 17), TaqMan® probe (SEQ ID NO: 18). Mn-SOD forward primer (SEQ ID NO: 19), reverse primer (SEQ ID NO: 20), TaqMan® probe (SEQ ID NO: 21).